

AMENDMENTS TO THE CLAIMS

Claim 1 (Currently amended): An isolated polypeptide that ameliorates a symptom of atherosclerosis or other pathology associated with an inflammatory response, said polypeptide comprising an amphipathic ~~helix helical peptide~~ having charged residues on the polar face of the peptide and possessing a wide non-polar face, wherein said polypeptide ranges in length from 10 amino acids to 40 amino acids, and wherein said polypeptide comprises the amino acid sequence DQYYLRVTTVA, (SEQ ID NO:18).

Claims 2-7 (Canceled).

Claim 8 (Currently amended): The polypeptide of claim 7~~1~~, wherein said polypeptide is a concatamer of two or more of said amino acid sequences.

Claim 9 (Currently amended): The polypeptide of claim 2~~1~~, wherein said polypeptide further comprises a protecting group.

Claim 10 (Currently amended): The polypeptide of claim 2~~1~~, wherein said polypeptide further comprises a protecting group coupled to the amino or carboxyl terminus.

Claim 11 (Currently amended): The polypeptide of claim 9, wherein said protecting group is a protecting group selected from the group consisting of ~~acetyl~~, amide, 3 to 20 carbon alkyl groups, Fmoc, ~~t-boc~~, 9-fluoreneacetyl group, 1-fluorenenecarboxylic group, ~~9-fluorenenecarboxylic~~ 9-fluorenenecarboxylic group, 9-fluorenone-1-carboxylic group, ~~benzyloxycarbonyl~~, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethylbenzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), ~~4,4-dimethoxybenzhydryl~~ 4,4-dimethoxybenzhydryl (Mbh), Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-dioxocyclohexylidene)dioxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzoyloxycarbonyl (2-Cl-Z), 2-bromobenzoyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), ~~a benzoyl group~~, a carbobenzoxy group, a propyl group, a butyl group, a pentyl group, a hexyl group, and Trifluoroacetyl (TFA).

Claim 12 (Currently amended): The polypeptide of claim 9, wherein said polypeptide comprises a protecting group coupled to the amino ~~terminal~~terminus and said amino terminal protecting group is a protecting group selected from the group consisting of a benzoyl group, an acetyl, a ~~propeonyl~~ propionyl, a carbobenzoxy, a propyl, a butyl, a pentyl, a hexyl, and a 3 to 20 carbon alkyl.

Claim 13 (Currently amended): The polypeptide of claim 9, wherein said polypeptide comprises a protecting group coupled to the carboxyl ~~terminal~~terminus and said carboxyl terminal protecting group is an amide.

Claim 14 (Currently amended): The polypeptide of claim 9, wherein said polypeptide further comprises:

a first protecting group coupled to the amino terminus wherein said protecting group is a protecting group selected from the group consisting of a benzoyl group, an acetyl, a ~~propeonyl~~ propionyl, a carbobenzoxy, a propyl, a butyl, a pentyl, a hexyl, and a 3 to 20 carbon alkyl; and

a second protecting group coupled to the carboxyl ~~terminal~~ terminus and said carboxyl terminal protecting group is an amide.

Claim 15 (Currently amended): The polypeptide of claim 21, wherein said polypeptide comprises a first protecting group coupled to the amino terminus and a second protecting group coupled to the carboxyl terminus.

Claim 16 (Currently amended): The polypeptide of claim 21, wherein said polypeptide comprises an Ac group on the amino terminus.

Claim 17 (Currently amended): The polypeptide of claim 21, wherein said polypeptide comprises an -NH₂ on the carboxyl terminus.

Claim 18 (Currently amended): The polypeptide of claim 21, wherein said polypeptide comprises an Ac group on the amino terminus and an -NH₂ on the carboxyl terminus.

Claim 19 (Currently amended): The polypeptide of claim 71, wherein said polypeptide comprises an Ac group on the amino terminus.

Claim 20 (Currently amended): The polypeptide of claim 71, wherein said polypeptide comprises an -NH₂ on the carboxyl terminus.

Claim 21 (Currently amended): The polypeptide of claim 71, wherein said polypeptide comprises an Ac group on the amino terminus and an -NH₂ on the carboxyl terminus.

Claim 22 (Currently amended): The polypeptide of claim 21, wherein said peptide comprises a "D" amino acid.

Claim 23 (Currently amended): The polypeptide of claim 21, wherein said peptide comprises a plurality of "D" amino acids.

Claim 24 (Currently amended): The polypeptide of claim 21, wherein all enantiomeric amino acids comprising said polypeptide are "D" amino acids.

Claim 25 (Currently amended): The polypeptide of claim 21, wherein said polypeptide is mixed with a pharmacologically acceptable excipient.

Claim 26 (Currently amended): The polypeptide of claim 21, wherein said peptide is mixed with a pharmacologically acceptable excipient suitable for oral administration to a mammal.

Claims 27-28 (Canceled).

Claim 29 (Original): The polypeptide of claim 1, wherein said polypeptide is coupled to a phospholipid.

Claim 30 (Original): The polypeptide of claim 29, wherein said polypeptide is covalently coupled to a phospholipid.

Claim 31 (Original): The polypeptide of claim 29, wherein said polypeptide is covalently coupled to a phospholipid comprising lysophosphatidyl choline.

Claim 32 (Currently amended): The polypeptide of claim 29, wherein said polypeptide is covalently coupled to a phospholipid comprising a fatty acid selected from the group consisting of propionoyl, butanoyl, pentanoyl, caproyl, heptanoyl, capryloyl, nonanoyl, capryl, ~~undecanoyl~~ undecanoyl, lauroyl, tridecanoyl, myristoyl, pentadecanoyl, palmitoyl, heptadecanoyl, stearoyl,

nonadecanoyl, arachidoyl, henicosanoyl, behenoyl, tricusanoyl, lignoceroyl, myristoleoyl (9-cis), myristelaidoyl (9-trans), palmitoleoyl (9-cis), and palmitelaidoyl (9-trans).

Claim 33 (Original): The polypeptide of claim 32, wherein said polypeptide is covalently coupled to the sn-1 or sn-2 position of said phospholipid.

Claim 34 (Currently amended): A composition suitable for oral administration that ameliorates a symptom of atherosclerosis, wherein said composition comprises a peptide comprising an amphipathic helix having charged residues on the polar face of the peptide and possessing a wide non-polar face, wherein said peptide comprises a D amino acid, said polypeptide ranges in length from 10 amino acids to 40 amino acids, said polypeptide comprises the amino acid sequence DQYYLRVTTVA, (SEQ ID NO:18), and said peptide is blocked at the amino terminus and the carboxyl terminus comprises a first protecting group coupled to the amino terminus and a second protecting group coupled to the carboxyl terminus.

Claim 35-40 (Canceled).

Claim 41 (Currently amended): The composition of claim ~~35~~34, wherein said first protecting group and said second protecting group are independently selected from the group consisting of ~~acetyl~~, amide, 3 to 20 carbon alkyl groups, Fmoc, ~~t-boc~~, 9-fluoreneacetyl group, 1-fluoreneacetyl group, ~~9-fluoreneacetyl~~9-fluoreneacetyl group, 9-fluorenone-1-carboxylic group, ~~benzyloxycarbonyl~~, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), ~~4,4-dimethoxybenzhydryl~~4,4-dimethoxybenzhydryl (Mbh), Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-dioxocyclohexylidene)dioxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzoyloxycarbonyl (2-Cl-Z), 2-bromobenzoyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), ~~a benzoyl group~~, a carbobenzoxy group, a propyl group, a butyl group, a pentyl group, a hexyl ~~group~~, and Trifluoroacetyl (TFA).

Claim 42 (Currently amended): The composition of claim ~~35~~34, wherein said first protecting group is an acetyl.

Claim 43 (Currently amended): The composition of claim ~~35~~34, wherein said second protecting group is an amide.

Claim 44 (Currently amended): The composition of claim ~~35~~34, wherein more than half of the enantiomeric amino acids comprising said peptide are D amino acids.

Claim 45 (Currently amended): The composition of claim ~~35~~34, wherein all enantiomeric amino acids comprising said peptide are D amino acids.

Claim 46 (Currently amended): The composition of claim ~~35~~34, wherein said composition further comprises a pharmaceutically acceptable excipient.

Claim 47 (Original): The composition of claim 46, wherein said excipient is an excipient suitable for oral administration.

Claim 48 (Original): The composition of claim 46, wherein said excipient is an excipient suitable for injection.

Claim 49 (Original): A pharmaceutical composition, said composition comprising a polypeptide of claim 1 in a pharmaceutically acceptable excipient.

Claim 50 (Currently amended): The composition of claim 49, wherein said composition ~~comprises~~ is in the form of a unit dosage formulation.

Claim 51 (Currently amended): The composition of claim ~~35~~34, wherein said ~~polypeptide~~ peptide is coupled to a phospholipid.

Claim 52 (Currently amended): The composition of claim 51, wherein said ~~polypeptide~~ peptide is covalently coupled to a phospholipid.

Claim 53 (Currently amended): The composition of claim 51, wherein said ~~polypeptide~~ peptide is covalently coupled to a phospholipid comprising lysophosphatidyl choline.

Claim 54 (Currently amended): The composition of claim 51, wherein said ~~polypeptide~~ peptide is covalently coupled to a phospholipid comprising a fatty acid selected from the group consisting of propionoyl, butanoyl, pentanoyl, caproyl, heptanoyl, capryloyl, nonanoyl, capryl, undecanoyl, ~~undecanoyl~~, lauroyl, tridecanoyl, myristoyl, pentadecanoyl, palmitoyl, heptadecanoyl,

stearoyl, nonadecanoyl, arachidoyl, henicosanoyl, behenoyl, truncanoyl, lignoceroyl, myristoleoyl (9-cis), myristelaidoyl (9-trans), palmitoleoyl (9-cis), and palmitelaidoyl (9-trans).

Claim 55 (Currently amended): A method of ameliorating a symptom of atherosclerosis in a mammal, said method comprising administering to said mammal a peptide or a concatamer of a peptide comprising an amphipathic helix helical peptide-having charged residues on the polar face of the peptide-helix and possessing a wide non-polar face on said helix, wherein said peptide ranges in length from 10 amino acids to 40 amino acids, and wherein said peptide comprises the amino acid sequence DQYYLRVTTVA, (SEQ ID NO:18).

Claims 56-61 (Canceled).

Claim 62 (Currently amended): The method of claim ~~64~~55, wherein said peptide is a concatamer of two or more of said amino acid sequences.

Claim 63 (Currently amended): The method of claim ~~56~~55, wherein said peptide further comprises a protecting group.

Claim 64 (Currently amended): The method of claim ~~56~~55, wherein said peptide further comprises a protecting group coupled to the amino or carboxyl terminus.

Claim 65 (Currently amended): The method of claim 63, wherein said protecting group is a protecting group selected from the group consisting of ~~acetyl~~, amide, 3 to 20 carbon alkyl groups, Fmoc, ~~t-boc~~, 9-fluoreneacetyl group, 1-fluorene-carboxylic group, ~~9-fluorene-carboxylic~~9-fluorene-carboxylic group, 9-fluorenone-1-carboxylic group, ~~benzyloxy-carbonyl~~, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), ~~4,4-dimethoxybenzhydryl~~4,4-dimethoxybenzhydryl (Mbh), Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-dioxocyclohexylidene)dioxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzoyloxycarbonyl (2-Cl-Z), 2-bromobenzoyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), ~~a benzoyl group~~, a carbobenzoxy group, a propyl group, a butyl group, a pentyl group, a hexyl group, and Trifluoroacetyl (TFA).

Claim 66 (Currently amended): The method of claim 63, wherein said peptide comprises a protecting group coupled to the amino terminal and said amino ~~terminal~~ terminus protecting group is a protecting group selected from the group consisting of a benzoyl group, an acetyl, a ~~propeonyl~~ propionyl, a carbobenzoxy, a propyl, a butyl, a pentyl, a hexyl, and a 3 to 20 carbon alkyl.

Claim 67 (Currently amended): The method of claim 63, wherein said peptide comprises a protecting group coupled to the carboxyl ~~terminal~~ terminus and said carboxyl terminal protecting group is an amide.

Claim 68 (Currently amended): The method of claim 63, wherein said peptide further comprises:

a first protecting group coupled to the amino terminus wherein said protecting group is a protecting group selected from the group consisting of a benzoyl group, an acetyl, a ~~propeonyl~~ propionyl, a carbobenzoxy, a propyl, a butyl, a pentyl, a hexyl, and a 3 to 20 carbon alkyl; and

a second protecting group coupled to the carboxyl ~~terminal~~ terminus and said carboxyl terminal protecting group is an amide.

Claim 69 (Currently amended): The method of claim ~~5655~~, wherein said peptide comprises a first protecting group coupled to the amino terminus and a second protecting group coupled to the carboxyl terminus.

Claim 70 (Currently amended): The method of claim ~~5655~~, wherein said peptide comprises an Ac group on the amino terminus.

Claim 71 (Currently amended): The method of claim ~~5655~~, wherein said peptide comprises an --NH₂ on the carboxyl terminus.

Claim 72 (Currently amended): The method of claim ~~5655~~, wherein said peptide comprises an Ac group on the amino terminus and an --NH₂ on the carboxyl terminus.

Claims 73-75 (Canceled).

Claim 76 (Currently amended): The method of claim ~~5655~~, wherein said peptide comprises a "D" amino acid.

Claim 77 (Currently amended): The method of claim ~~56~~55, wherein said peptide comprises a plurality of "D" amino acids.

Claim 78 (Currently amended): The method of claim ~~56~~55, wherein all enantiomeric amino acids comprising said peptide are "D" amino acids.

Claim 79 (Currently amended): The method of claim ~~56~~55, wherein said ~~polypeptide~~ is coupled to a phospholipid.

Claim 80 (Currently amended): The method of claim 79, wherein said ~~polypeptide~~ is covalently coupled to a phospholipid.

Claim 81 (Currently amended): The method of claim 79, wherein said ~~polypeptide~~ is covalently coupled to a phospholipid comprising lysophosphatidyl choline.

Claim 82 (Currently amended): The method of claim 79, wherein said ~~polypeptide~~ is covalently coupled to a phospholipid comprising a fatty acid selected from the group consisting of propionoyl, butanoyl, pentanoyl, caproyl, heptanoyl, capryloyl, nonanoyl, capryl, undecanoyl ~~undeanoyl~~, lauroyl, tridecanoyl, myristoyl, pentadecanoyl, palmitoyl, heptadecanoyl, stearoyl, nonadecanoyl, arachidoyl, henicosanoyl, behenoyl, tricusanoyl, lignoceroyl, myristoleoyl (9-cis), myristelaidoyl (9-trans), and palmitoleoyl (9-cis), palmitelaidoyl (9-trans).

Claim 83 (Currently amended): The method of claim ~~56~~55, wherein said peptide is mixed with a pharmacologically acceptable excipient.

Claim 84 (Currently amended): The method of claim ~~56~~55, wherein said peptide is mixed with a pharmacologically acceptable excipient suitable for oral administration to a mammal.

Claim 85 (Original): The method of claim 55, wherein said administering comprises orally administering said peptide.

Claim 86 (Original): The method of claim 55, wherein said mammal is a mammal diagnosed as having one or more symptoms of atherosclerosis.

Claim 87 (Currently amended): The method of claim 55, wherein said ~~organism-mammal~~ is a mammal diagnosed as at risk for atherosclerosis.

Claim 88 (Original): The method of claim 55, wherein said mammal is a human.

Claim 89 (Original): The method of claim 55, wherein said mammal is non-human mammal.

Claim 90 (Currently amended): A method of ameliorating a symptom of a pathology characterized by an inflammatory response in a mammal, said method comprising administering to said mammal a peptide or a concatamer of a peptide comprising an amphipathic ~~helical peptide~~ helix having charged residues on the polar face ~~of the peptide~~ and possessing a wide non-polar face, wherein said polypeptide ranges in length from 10 amino acids to 40 amino acids, and wherein said polypeptide comprises the amino acid sequence DQYYLRVTTVA, (SEQ ID NO:18).

Claims 91-96 (Canceled).

Claim 97 (Currently amended): The method of claim ~~91~~90, wherein said ~~organism-mammal~~ is an-organism- a mammal diagnosed as having one or more symptoms of an inflammatory response.

Claim 98 (Currently amended): The method of claim ~~91~~90, wherein said ~~organism-mammal~~ is an-organism- a mammal diagnosed as at risk for a pathology associated with an inflammatory response.

Claim 99 (Currently amended): The method of claim ~~91~~90, wherein said ~~organism-mammal~~ is a human.

Claim 100 (Currently amended): The method of claim ~~91~~90, wherein said ~~organism-mammal~~ is non-human mammal.

Claim 101 (Currently amended): A kit for ameliorating a symptom of atherosclerosis, said kit comprising a container containing a polypeptide of any one of claims 1, and 8-26. 1 through 28.

Claim 102 (Currently amended): The kit of claim 101, wherein said polypeptide is combined with a pharmaceutically acceptable excipient.

Claim 103 (Currently amended): The kit of claim 101, wherein said polypeptide is combined with a pharmaceutically acceptable excipient in a unit dosage formulation.

Claim 104 (Original): The kit of claim 103, wherein said unit dosage formulation is for oral administration.

Claim 105 (Original): The kit of claim 101, further comprising instructional materials teaching the use of said peptide for ameliorating one or more symptoms of atherosclerosis or of a pathology characterized by an inflammatory response.

Claim 106 (Currently amended): A method of mitigating or preventing a coronary complication associated with an acute phase response to an inflammation in a mammal, ~~wherein said coronary complication is a symptom of atherosclerosis~~, said method comprising administering to a mammal having said acute phase response, or at risk for said acute phase response, a polypeptide of any one of claims 1, and 8-26. ~~1 through 28~~.

Claim 107 (Currently amended): The method of claim 106, where said administration is by a route selected from the group consisting of oral administration, nasal administration, rectal administration, intraperitoneal injection, ~~and~~ intravascular injection, subcutaneous injection, transcutaneous administration, and intramuscular injection.

Claim 108 (Original): The method of claim 106, wherein said polypeptide is administered in combination with an all L-form of the same polypeptide.

Claim 109 (Original): The method of claim 106, wherein said polypeptide is provided as a unit formulation in a pharmaceutically acceptable excipient.

Claim 110 (Original): The method of claim 106, wherein said acute phase response is an inflammatory response associated with a recurrent inflammatory disease.

Claim 111 (Currently amended): The method of claim 107, wherein said acute phase response is associated with a disease selected from the group consisting of leprosy, tuberculosis, systemic lupus erythematosus, polymyalgia rheumatica, polyarteritis nodosa, scleroderma, idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, ~~Alzheimers Disease and AIDS, polymyalgia rheumatica, polyarteritis nodosa, scleroderma, idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, Alzheimers Disease, AIDS,~~ coronary calcification, calcific aortic stenosis, osteoporosis, and rheumatoid arthritis.

Claim 112 (Original): The method of claim 106, wherein said acute phase response is an inflammatory response associated with a condition selected from the group consisting of a bacterial

infection, a viral infection, a fungal infection, an organ transplant, a wound, an implanted prosthesis, parasitic infection, sepsis, endotoxic shock syndrome, and biofilm formation.

Claim 113 (Currently amended): A method of mitigating or preventing a coronary complication associated with an acute phase response to an inflammation in a mammal, ~~wherein said coronary complication is a symptom of atherosclerosis~~, said method comprising:

assaying said mammal for an acute phase protein (APP) level indicative of an acute phase response or a significant risk of an acute phase response; and

administering to a mammal showing an acute phase protein (APP) level indicative of an acute phase response a polypeptide of any one of claims 1, and 8-26.1 through 28.

Claim 114 (Currently amended): The method of claim 113, wherein said acute phase protein (APP) is a ~~positive~~ positive APR selected from the group consisting of serum amyloid A, c-reactive protein, serum amyloid P component, C2 complement protein, C3 complement protein, C4 complement protein, C5 complement protein, C9 complement protein, B complement protein, C1 inhibitor, C4 binding protein, fibrinogen, von Willebrand factor, α 1-antitrypsin, α 1-antichymotrypsin, α 2 antiplasmin, heparin cofactor II, plasminogen activator inhibitor I, haptoglobin, haemopexin, ceruloplasmin, manganese superoxide dismutase, α 1-acid glycoprotein, haeme oxygenase, mannose binding protein, leukocyte protein I, lipoprotein (a), and lipopolysaccharide binding protein.

Claim 115 (Currently amended): The method of claim 113, wherein said acute phase protein (APP) is a negative APR selected from the group consisting of albumin, prealbumin, transferin, apoAI, apoAII, α 2-HS glycoprotein, inter- α -trypsin inhibitor, and ~~histidine-rich~~ glycoprotein.